REMARKS

Claims 1, 33, 34, 35 and 38 have been amended A marked version of the claims indicating the changes to the claims is attached hereto as Exhibit A. A copy of all the claims, as amended, is attached hereto as Exhibit B. The amendments regarding DS-CAM cDNA, and the complement of a sequence encoding a DS-CAM polypeptide are fully supported by the present specification, see, *e.g.*, page 12, lines 20 to page 13, line 2. No new subject matter is introduced.

Applicants acknowledge that the Examiner found claims 44-46 allowable.

1. The Rejections Under 35 U.S.C. § 102 Are Obviated

Claim 1 stands rejected under 35 U.S.C. 102(a) as being anticipated by Korenberg, et al. (*PNAS USA*, 91;4997-5001, 1994, "Korenberg").

The Examiner points out that claim 1 recites a nucleic acid molecule and uses the term "comprising" which is open-ended language. The Examiner maintains that the recitation of claim 1 would be encompassed by the reference teaching and therefore, the rejection stands. Applicants traverse the Examiner's assertion that Korenberg discloses the nucleic acid molecule of rejected claim 1. In the interest of expediting prosecution, Applicants have amended claim 1 to replace the term "comprising" with "consisting essentially of". The phrase "consisting essentially of" is a term of art defined in § 2111.03 of the Manual of Patent Examining Procedure (Seventh Edition, Revision 1). When included in a claim, the term limits the scope of the claim to the specified materials or steps and those that do not materially affect the basic and novel charateristic(s) of the claimed invention. No new matter is introduced and the amendment is fully supported by the specification as filed. As such, Applicants submit that the amended claim 1 obviates the rejection based on Korenberg, and request the withdrawal of the rejection.

Claims 33-35, 38 and 41 are rejected under 35 U.S.C. 102(a) as being anticipated by Korenberg, et al. (PNAS USA, 91:4997-5001, 1994). Allegedly, Korenberg teaches an isolated nucleic acid obtained from patients with Down Syndrone, and DS-CAM would inherently be encoded by nucleic acids taught by Korenberg. The Examiner contends that the chromosomal DNA isolated for Southern blot analysis, as taught on page 4998 would be expected to hybridize to SEQ ID NO: 1 under the recited conditions, absent evidence to the contrary. Applicants respectfully disagree with the Examiner's contention.

In response, Applicants reiterate that Korenberg does not disclose any particular DNA molecule that is identified to be encoding DS-CAM. The Examiner's assertion that the claimed nucleic acids would inherently be encoded by nucleic acid taught by Korenberg amounts to a rejection based solely on the existence of a pool of DNA fragments derived from a chromosome which is known to contain at least a gene which is associated with Down's syndrome but also thousands of other known and unknown genes. Applicants' claims are not directed to a pool of nucleic acid molecules in which one may encode DS-CAM. The rejection is thus in error.

Moreover, with respect to claim 41, Applicants respectfully point out that the recited nucleotide sequences (i.e., SEQ ID No: 1, 7, 8, 9 and 10) are complementary DNA (cDNA) sequences (see page 63 of the specification) and do not comprise any intervening (or intron) sequences, or chromosomal sequences. Therefore, the rejection of claim 41 is in error.

Without admitting that the nucleic acids of rejected claims 33, 34, 35 and 38 are taught in Korenberg, claims 33, 34, 35 and 38 have been amended to specify that the recited nucleotide sequence is one that is of a cDNA, and thus would not include any intron sequences. Applicants respectfully point out that Korenberg does not disclose any isolated cDNA molecules or fragments thereof that are associated with DS-CAM. Furthermore, there is no disclosure in Korenberg of any isolated chromosomal DNA molecule that does not comprise intron sequence, and that encodes DS-CAM or hybridizes to DS-CAM. The claims have also been amended to recite that the cDNA hybridizes to the complement of a coding sequence. Applicants submit that the rejections of claims 33, 34, 35 and 38 are obviated.

Claims 33-37, 47 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Genexpress cDNA Program (GenBank, Accession #F13426).

Applicants submit that the Genbank sequence accession #F13426 discloses a 309 bp fragment of nucleic acid which overlaps with SEQ ID NO: 1 starting from nucleotides 5280 to 5589 which encodes 1610 to 1712 of the amino acid sequence of SEQ ID NO: 2. F13426 also overlaps with SEQ ID NO: 10 starting from nucleotides 5133 to 5398, part of which encodes the terminal portion of the amino acid sequence of SEQ ID NO: 11 from 1561 to 1571.

In response, Applicants have amended claim 33 to recite that the second nucleic acid consists of a nucleotide sequence that encodes residue 1 to 1473 of the amino

acid sequence of SEQ ID NO: 11. Applicants submit that the claim amendment is supported by Figure 3 and the sequence listing. The recited amino acid sequence of SEQ ID NO:11 from residue 1 to 1473 represents all the amino acid residues encoded by exon sequences upstream of the exon that consists of the 5' end of the alternative splice site as illustrated in Figure 3. The alternative splice site occurs at nucleotides 5132 of SEQ ID NO. 1 and 10, resulting in the removal of nucleotides 5133-5323 of SEQ ID NO. 1. As shown in Figure 3, the exon that consists of the alternative splice site and that has 294 bp starts with nucleotide 4873 which encodes amino acid residue 1474 of SEQ ID NO: 2 and 11. Accordingly, Figure 3 identifies the boundaries of the exon that consists of the 5' end of the alternative splice site and provides support for the claim amendment.

As a result of the amendment, there is no overlap in sequence between F13426 and the second nucleic acid molecule to which the claimed nucleic acid of claim 33 hybridizes. As such, F13426 will not hybridize to the second nucleic acid of claim 33. Applicants submit that the rejection of claim 33 is obviated and should thus be withdrawn.

With respect to claim 34, Applicants point out that there is no overlap between F13426 and either of the nucleotide sequences encoding the two recited regions of SEQ ID NO: 2, namely residues 24 to 126, and residues 1069 to 1185. As stated above, F13426 overlaps with nucleotide sequences of SEQ ID NO: 1 that encodes 1610 to 1712 of the amino acid sequence of SEQ ID NO: 2. As such, F13426 will not hybridize to either of the recited nucleotide sequences. Applicants submit that the rejection of claim 34 is in error.

With respect to claim 35, Applicants point out that there is no overlap between F13426 and either SEQ ID NO: 7 or 8. The nucleotide sequence of SEQ ID NO: 7 (from 1 to 842) aligns with SEQ NO: 1 in a region from around nucleotide 360 to 1190. The nucleotide sequence of SEQ ID NO: 8 (from 1 to 898) aligns with SEQ NO: 1 in the reverse orientation in a region from around nucleotide 3650 to 2750. As described above, F13426 overlaps and will hybridizes with SEQ ID NO: 1 from nucleotides 5280 to 5589. Thus, F13426 will not hybridize to either of the recited nucleotide sequences in claim 35. Applicants submit that the rejection of claim 35 is in error.

In view of the foregoing, the rejections of claims 1, 33-38, 41, 47 and 48 should be withdrawn.

2. The Rejection Under 35 U.S.C. § 103 Are Obviated

Claims 1, 31-43 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Korenberg et al. (*PNAS USA*, 91 4997-5001, 1994), in view of Gallatin, et al., (US Patent No. 5,535,487). The Examiner alleges that one of ordinary skill in the art at the time of the invention was made would have been motivated to use the DNA taught by Korenberg in a method for expression of a DS-CAM related protein, in order to produce large quantities of the protein.

In response, Applicants respectfully point out that Korenberg, as discussed above, does not disclose isolated nucleic acid molecules that encode DS-CAM or hybridize to the DS-CAM gene. Korenberg merely teaches a pool of chromosomal DNA fragments which was shown to contain genes associated with Down'syndrome. However, there was no disclosure of the identification of any cell adhesion molecules in Korenberg. Gallatin teaches methods of making a cell adhesion molecule polypeptide but there is no indication that any of the expressed cell adhesion molecules is involved in Down's syndrome. Accordingly, there is no suggestion of the claimed nucleic acids, vectors, and cells. Nor is there suggestion or motivation in either reference to combine the teachings of the other reference. In view of the teachings of Korenberg and Gallatin, one of ordinary skill in the art would not reasonably expect success in expressing DS-CAM or DS-CAM related polypeptides, let alone large (or any useful) quantities of the protein or polypeptide. As such, the rejection is in error and should be withdrawn.

Claims 33-37 and 47-49 are rejected under 35 U.S.C. 103(a) as being patentable over Genexpress cDNA Program (GenBank, Accession #F13426), in view of Gallatin, et al., (US Patent No. 5,525,487). The Examiner alleges that one of ordinary skill in the art at the time the invention was made would have been motivated to use the DNA taught by #F13426 in a method for expression of a DS-CAM related protein in view of Gallatin. Applicants respectfully disagree.

As described above, the Genbank sequence #F13426 does not disclose identically the claimed nucleic acid molecules. #F13426 does not encode a cellular adhesion molecule, such as that taught in Gallatin. Rather, the Genebank sequence merely teaches a nucleic acid fragment encoding a peptide fragment which has no known function. Thus, contrary to the Examiner's assertion, there is no motivation, absent the teachings of the present specification, to combine this sequence with the teachings of Gallatin to render the presently claimed invention obvious.

Thus, in view of the above-made arguments and amendments, Applicant respectfully requests that the rejection under 35 U.S.C. § 103(a) be withdrawn.

3. The Rejection Under 35 U.S.C. § 112 Are Obviated

Claims 33, 34, 36, 37, 47 and 48 are rejected under 35 U.S.C. 112, first paragraph, for lack of written description. The Examiner alleges that there is insufficient support in the specification for the recitation in claim 33 for "intronless", and there is also insufficient support for the limitation in claim 34 for the recitation of hybridization to a second and third nucleic acid molecule. Applicants respectfully traverse.

In response, Applicants point out that in claim 33, in lieu of "intronless", the amended claim recites that the nucleic acid molecule comprise the sequence of a complementary DNA (see support at page 12, line 30 to page 13, line 2.) This rejection of claim 33 is thus obviated.

With respect to the limitation in claim 34, Applicants respectfully direct the Examiner's attention to page 17 of the specification, lines 17-24, wherein it is stated that the preferred nucleic acids according to the invention hybridize to substantial portions of the nucleic acid sequences set forth in SEQ ID NO: 1, 7, 8, 9, and 10. Thus, the rejection is in error.

Claims 33, 36, 37, 47 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The Examiner alleges that it is unclear from the claims and from Applicants' remarks in Paper No. 20, whether the Applicants intend to claim a nucleic acid molecule which hybridizes to 2 separate molecules concurrently, or whether the claim is drawn to a nucleic acid molecule which binds to a separate, second molecule. Claim 33 has been amended and Applicants respectfully submit that the claimed isolated nucleic acid binds to a separate second nucleic acid by molecular hybridization under high stringency conditions. The amended claim and the claims dependent therefrom do not lack clarity and the rejection is thus obviated.

In view of the foregoing, Applicants submit that the rejection under § 112 should be withdrawn.

Conclusion

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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EXHIBIT A
MARKED VERSION OF THE CLAIMS
U.S. PATENT APPLICATION SERIAL NO. 09/956,991

1 (amended). An isolated nucleic acid consisting essentially of [comprising] (a) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or 11; and (b) the complement of the nucleotide sequence of (a).

33 (amended). An isolated [intronless] nucleic acid comprising the [a] nucleotide sequence of a complementary DNA which hybridizes under high stringency conditions to the complement of a second nucleic acid encoding the amino acid sequence set forth in SEQ ID NO:11, wherein said high stringency conditions comprise hybridizing in 5X Denhardt's solution, 5X SSPE and 0.2% sodium dodecylsulfate at 42°C, followed by washing in 0.1X SSPE and 0.1% Sodium dodecylsulfate at 65°C.

34 (amended). An isolated nucleic acid comprising the nucleotide sequence of a complementary DNA that [which] hybridizes under high stringency conditions to the complement of a second nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:1 that encodes amino acids 24 to 126 of SEQ ID NO:2 and that hybridizes under high stringency conditions to the complement of a third nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:1 that encodes amino acids 1069 to 1185 of SEQ ID NO:2, wherein said high stringency conditions comprise hybridizing in 5X Denhardt's solution, 5X SSPE and 0.2% sodium dodecylsulfate at 42°C, followed by washing in 0.1X SSPE and 0.1% Sodium dodecylsulfate at 65°C.

35 (amended). An isolated nucleic acid comprising the [a] nucleotide sequence of a complementary DNA which hybridizes under high stringency conditions to the complement of a second nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:7 or SEQ ID NO:8, wherein said high stringency conditions comprise hybridizing in 5X Denhardt's solution, 5X SSPE and 0.2% sodium dodecylsulfate at 42°C, followed by washing in 0.1X SSPE and 0.1% Sodium dodecylsulfate at 65°C.

38 (amended). An isolated nucleic acid comprising the [a] nucleotide sequence of a complementary DNA which encodes a polypeptide comprising at least one of the amino

acid sequences selected from the group consisting of: amino acids 1-23, 24-126, 127-225, 226-316, 317-409, 410-506, 507-603, 604-697, 698-792, 793-887, 888-983, 984-1067, 1068-1185, 1186-1281, 1282-1375, 1376-1471, 1472-1594, 1595-1616, and 1617-1910 of SEQ ID NO:2.

EXHIBIT B

THE CLAIMS WHICH WILL BE PENDING

UPON ENTRY OF THE PRESENT AMENDMENT

U.S. PATENT APPLICATION SERIAL NO. 09/956,991

1 (amended). An isolated nucleic acid consisting essentially of (a) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or 11; and (b) the complement of the nucleotide sequence of (a).

31. A vector comprising the isolated nucleic acid of claim 1.

32. An isolated cell containing the nucleic acid of claim 1 or 31.

33 (amended). An isolated nucleic acid comprising the nucleotide sequence of a complementary DNA which hybridizes under high stringency conditions to the complement of a second nucleic acid encoding the amino acid sequence set forth in SEQ ID NO:11, wherein said high stringency conditions comprise hybridizing in 5X Denhardt's solution, 5X SSPE and 0.2% sodium dodecylsulfate at 42°C, followed by washing in 0.1X SSPE and 0.1% Sodium dodecylsulfate at 65°C.

34 (amended). An isolated nucleic acid comprising the nucleotide sequence of a complementary DNA that hybridizes under high stringency conditions to the complement of a second nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:1 that encodes amino acids 24 to 126 of SEQ ID NO:2 and that hybridizes under high stringency conditions to the complement of a third nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:1 that encodes amino acids 1069 to 1185 of SEQ ID NO:2, wherein said high stringency conditions comprise hybridizing in 5X Denhardt's solution, 5X SSPE and 0.2% sodium dodecylsulfate at 42°C, followed by washing in 0.1X SSPE and 0.1% Sodium dodecylsulfate at 65°C.

35 (amended). An isolated nucleic acid comprising the nucleotide sequence of a complementary DNA which hybridizes under high stringency conditions to the complement of a second nucleic acid consisting of the nucleotide sequence set forth in SEQ ID NO:7 or

SEQ ID NO:8, wherein said high stringency conditions comprise hybridizing in 5X Denhardt's solution, 5X SSPE and 0.2% sodium dodecylsulfate at 42°C, followed by washing in 0.1X SSPE and 0.1% Sodium dodecylsulfate at 65°C.

36. A vector comprising the isolated nucleic acid of claim 33, 34, or 35.

37. An isolated cell containing the nucleic acid of claim 33, 34, or 35.

38 (amended). An isolated nucleic acid comprising the nucleotide sequence of a complementary DNA which encodes a polypeptide comprising at least one of the amino acid sequences selected from the group consisting of: amino acids 1-23, 24-126, 127-225, 226-316, 317-409, 410-506, 507-603, 604-697, 698-792, 793-887, 888-983, 984-1067, 1068-1185, 1186-1281, 1282-1375, 1376-1471, 1472-1594, 1595-1616, and 1617-1910 of SEQ ID NO:2.

39. A vector comprising the isolated nucleic acid of claim 38.

40. An isolated cell containing the nucleic acid of claim 38 or 39.

41. An isolated nucleic acid molecule comprising a nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, nucleotides 453-6185 of SEQ ID NO:1 or nucleotides 453-5168 of SEQ ID NO:1.

42. A vector comprising the isolated nucleic acid of claim 41.

43. An isolated cell containing the nucleic acid of claim 41 or 42.

44. An oligonucleotide comprising at least 15 nucleotides of (a) a nucleotide sequence that encodes the polypeptide of SEQ ID NO:11; (b) the nucleotide sequence set forth in SEQ ID NO. 7 or 8; or (c) the complement of the nucleotide sequence of (a) or (b).

45. The oligonucleotide of claim 44 wherein the oligonucleotide sequence consists essentially of SEQ ID NO:5 or SEQ ID NO:6.

46. A kit for detecting the presence of a nucleic acid in a sample comprising in a package at least one oligonucleotide of claims 44 or 45.

47. The isolated nucleic acid of claim 1, 33, 34, 35, 38 or 41 which is cDNA.

48. The isolated nucleic acid of claim 1, 33, 34, 35, 38 or 41 which is RNA.

49. A method for making of a Down Syndrome-Cell Adhesion Molecule polypeptide or fragment thereof, said method comprising the steps of culturing the cell of claim 32, 37, 40 or 43 under conditions suitable for expression of said Down Syndrome-Cell Adhesion Molecule protein, and isolating the expressed Down Syndrome-Cell Adhesion Molecule protein.